To test if EphA2 could be stimulated by an agonist, MCF^{EphA2} cells were suspended in soft agar in the presence or absence of 0.5 mg/mL EphrinA1-F_c. EphrinA1-F_c increased the phosphotyrosine content of EphA2, and EphrinA1-F_c-treated cells exhibited reduced colony formation in soft agar by 49% relative to vehicle-treated controls ($P < 5x10^{-6}$). To test if EphA2 stimulation could alter cell behavior on Matrigel, the MCF^{EphA2} cells were treated with 0.5 mg/mL EphrinA1-F_c, which restored a spherical phenotype that was comparable to non-transformed MCF-10A cells. Thus, EphA2 stimulation reverses the effects of EphA2 overexpression. Despite its inability to interact with its endogenous ligands, the EphA2 in MCF^{EphA2} cells responded to exogenous stimuli.

In the Claims

Please amend claims 58, 62, 64, 66, 69, 72, 76, 79, 81, 84, 86, 89, 92, 95, and 98. The amended claims are provided below in clean form. Pursuant to 37 C.F.R. §1.121, amended claims are also shown in Appendix A with notations to indicate changes made (for convenience, all pending claims, including those added hereby, are provided in Appendix A).

58. (Amended) A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of a compound that increases the phosphotyrosine content of EphA2, wherein said administration reduces metastasis.

62. (Amended) A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of a compound that increases the phosphotyrosine content of EphA2, wherein said administration impedes proliferation of said metastatic cells.

C10

64. (Amended) A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of a compound that increases the phosphotyrosine content of EphA2 in said metastatic cells as compared to untreated metastatic cells.

C11

66. (Amended) A method for reducing the invasiveness of a metastatic cancer cell that expresses EphA2, the method comprising contacting the metastatic cell with a compound that increases the phosphotyrosine content of EphA2, thereby reducing the invasiveness of the metastatic cell compared to an untreated metastatic cell.

C12

69. (Amended) A method for reducing the proliferative behavior of a metastatic cancer cell that expresses EphA2, the method comprising contacting the metastatic cancer cell with a compound that increases the phosphotyrosine content of EphA2, thereby reducing the proliferative behavior of said metastatic cell compared to an untreated metastatic cell.

C13

72. (Amended) A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of an anti-EphA2 antibody that increases the phosphotyrosine content of EphA2, wherein said administration reduces metastasis.

C14

76. (Amended) The method of claim 72 wherein the anti-EphA2 antibody is a monoclonal antibody.

C15

79. (Amended) A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of an anti-EphA2 antibody that

C15 increases the phosphotyrosine content of EphA2, wherein said administration impedes proliferation of said metastatic cells.

C16 81. (Amended) The method of claim 79 wherein the anti-EphA2 antibody is a monoclonal antibody.

84. (Amended) A method for treatment of a patient having a metastatic tumor, said tumor C17 comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of an anti-EphA2 antibody that increases the phosphotyrosine content of EphA2 in said metastatic cells as compared to untreated metastatic cells.

C18 86. (Amended) The method of claim 84 wherein the anti-EphA2 antibody is a monoclonal antibody.

89. (Amended) A method for reducing the invasiveness of a metastatic cancer cell that C19 expresses EphA2, the method comprising contacting the metastatic cell with an anti-EphA2 antibody that increases the phosphotyrosine content of EphA2, thereby reducing the invasiveness of the metastatic cell compared to an untreated metastatic cell.

C20 92. (Amended) The method of claim 89 wherein the anti-EphA2 antibody is a monoclonal antibody.

C21 95. (Amended) A method for reducing the proliferative behavior of a metastatic cancer cell that expresses EphA2, the method comprising contacting the metastatic cancer cell with an anti-EphA2 that increases the phosphotyrosine content of EphA2, thereby reducing the proliferative behavior of said metastatic cell compared to an untreated metastatic cell.

98. (Amended) The method of claim 97 wherein the anti-EphA2 antibody is a monoclonal antibody.